and/or anti-diarrheal effect and/or promoting digestion, dissolution and/or absorption of an active ingredient.

With respect to compositions of matter, Claims 96 - 108 are directed to absorption promoting and/or gastric emptying slowing compositions. Claims 114-127, 137 and 138 are directed to anti-atherogenic, anti-diarrheal, digestion, dissolution and/or absorption promoting and/or gastrointestinal transit slowing and/or gastric emptying slowing compositions.

The Office Action

In the Office Action mailed on August 26, 2002, the Examiner acknowledged that Applicant's Request for Corrected Filing Receipt filed December 26, 2001, Request of Extensions of time filed December 26, 2001 and April 30, 2002, and Amendment And Request For Reconsideration And Withdrawal Of Restriction Requirement Under 37 C.F.R. § 1.143 filed June 13, 2002 have been received and entered by the Office.

The Examiner also acknowledged that Applicant's election with traverse of specie (a) capsule and Group II by paper dated April 18, 2002 has been entered and considered. In view of Applicant's Request for Reconsideration and Request for Withdrawal of Restriction Requirement, the Examiner has rejoined claim Groups I and II. Claims 131-136 were withdrawn from consideration by the Examiner, over traversal by the Applicant.

No claims were allowed.

The Examiner rejected Claims 96-130, 137, and 138 on the following grounds.

A. Rejections on Grounds of Obviousness-Type Double Patenting

The examiner rejected Claims 96 –130 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-32, 38-41, and 62 of the parent patent, U.S. Patent No. 5,977,175, because:

> **. . . Although the conflicting claims are not identical, they are not patentably distinct form each other because, they claimed the same subject matter, which is an 'anti--atherogenic, anti-diarrheal, digestion, dissolution and/or absorption promoting and/or gastrointestinal transit slowing and/or gastric emptying slowing' formulation.**

As the cited parent patent and the present application are both owned by Applicant herein, enclosed herewith is a terminal disclaimer executed by Applicant, disclaiming any part of the patent term that extends beyond the term of the parent patent. 37 C.F.R. 1.321(c).

In view of the above, Applicant respectfully submits that the above rejection has been overcome. As this is the only ground for rejection cited against Claims 97, 107-113, 115, and 126-130, Applicant further submits that these claims are now in condition for allowance.

B. Rejections under 35 U.S.C. § 102

The Examiner rejected Claims 96, 98-106, 114, 116, 117, 119-125, 137, and 138, as being anticipated by U.S. Patent No. 4,572,833 granted to Pedersen *et al.*, because:

> **Pedersen teaches controlled release composition[s] comprising multiple-unit[s] of active substance being coated with [a] hydrophobic layer (abstract and column 3). The hydrophobic material can be selected from oils, waxes, fats, including higher fatty acids, and mixtures thereof (column 4). Active substance, dosage form and coating agent are disclosed in columns 6-8.**

A claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference. *Verdgaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

In light of the aforementioned legal standard, Applicant respectfully disagrees that Pedersen *et al.* teaches all of the elements of the subject claims.

By way of background, Applicant provides the following general remarks explaining some of the novel aspects of the subject claims. Without wishing to be bound by any one theory, the inventive compositions in the pending claims include the following at least three novel aspects. First, the present claimed compositions are directed at manipulating the physiologic

reflex response of the gut, specifically, the response of the proximal small intestine known as the jejunal brake. Following the stomach and preceding the large bowel (colon) is the small intestine, which comprises three regions: the duodenum, jejunum, and ileum. A major function of the small intestine is one of absorption of digested nutrients. (*See* Specification at pg.1:13-16.) The speed of transit through the small intestine is normally regulated by inhibitory mechanisms located in the proximal and distal small intestine known as the jejunal brake and the ileal brake. Inhibitory feedback is activated to slow transit when end products of digestion make contact with nutrient sensors of the small intestine. (*See* Specification at pg. 4:3-6.) The desired effect of increased assimilation of luminal contents is achieved by a composition that triggers the slowing of intestinal transit by activating this jejunal brake. In contrast to previous efforts of the pharmaceutical industry, the focus is not only on the "formulation" (*i.e.*, how fast the active drug is released) but also the response of the gastrointestinal tract to the inventive composition. This focus on the response of the gut environment is completely novel.

A second novelty in the claimed compositions is that the intestinal slowing response is "jump-started" by delivering in the inventive composition end products of digestion (*i.e.*, "active lipids") rather than waiting for the normal process of digestion to make available the trigger for the slowing of intestinal transit (and thereby delaying gastric emptying).

A third novelty in the claimed compositions is that these "active lipids" can be consumed by mouth by the subject to evoke this response. Taken together these aspects are novel in light of the known art.

The aforementioned novel aspects are realized by a composition comprised, in part, of an "active lipid." (*See, e.g.,* Claims 96 and 114). That is, included as an element in each of the subject composition claims is an "active lipid," not lipids in general. The Specification specifically defines the term "active lipid" to encompass "a digested or substantially digested molecule having a structure and function substantially similar to a hydrolyzed end-product of fat digestion. Examples of hydrolyzed end products are molecules such as glycerol and fatty acids." (Specification at page 12, lines 10-13). These "end-products" of fat digestion include only fully hydrolyzed fats, such as fatty acids and glycerol, which would not include lipids in every form in which they occur. The desired intestinal slowing response is "jump-started" by delivering the

claimed compositions comprising end products of digestion, rather than waiting for the normal process of digestion to make available the trigger for the slowing of intestinal transit. Thus, the near immediate availability of the "active lipid" composition is important to accomplishing the desired result.

In contrast, Pedersen *et al.* teaches the formulation of a coating for preventing an active drug from being released all at once into the stomach. In order to accomplish this, Pedersen *et al.* discloses the use of a composition comprised of "hydrocarbons, waxes, oils and fats and mixtures thereof." (Pedersen *et al.* Col. 4:68-Col. 4:2.) Pedersen *et al.* goes on to disclose "higher fatty acids" as examples of "wax-like substances" called for by the described controlled release coating formulation. In essence, Pedersen *et al.* teaches the use of a coating comprised of a wax and a film-forming substance, among others, which together act as a barrier to the immediate release of the active drug; instead, the drug is released along the entire GI tract including the colon.

The fatty acids in wax-like form taught by Pedersen *et al.*, however, would not qualify as "active lipids." When in a wax-like state – as defined below – fatty acids would not be in the nearly-immediately available form to jump-start the jejunal brake to slow passage of the target active ingredient (*e.g.*, drug or nutrient) through the small intestine to maximize absorption; thus, while in this wax-like state, the fatty acids would not be considered fully hydrolyzed or "active."

The term "wax" does not denote a chemical class of compound as such. Rather, wax is a technological umbrella concept for materials that behave like waxes, *i.e.*, which have: (1) a melting point of at least 40°C (as opposed to fats and oils); (2) a relatively low melt viscosity, non-stringing, but producing droplets (unlike most resins and plastics), and (3) no chemical decomposition at higher temperatures (which distinguishes them from natural resins). (*See* enclosed printout from <http://www.byk-cera.nl/english/mainwax.htm>, **Exhibit 1**.) As indicated above, fatty acids formulated with these chemical properties would not provide the desired jump-start of the jejunal brake, in all likelihood, any more than a mixture containing non-digested fatty acids, *i.e.*, non-active lipids.

On the other hand, such chemical properties are desirable in the Pedersen *et al.* formulation. That is, the Pedersen *et al.* formulation relies on the fact that the coating, including

the waxy substance, remains **intact** after enteral delivery so as to act as a barrier to release of the active ingredient while passing through the gastrointestinal tract. (*See* Pedersen *et al.* at Column 2, lines 39-46.) Thus, the fatty acids in wax form called for in Pedersen *et al.* would not be readily available form to trigger the jejunal break.

Consequently, Pedersen *et al.*, at the very least, fails to teach a composition comprised of an "active lipid" – a limitation expressly required in each of independent composition Claims 96 and 114, and the claims that depend therefrom.

Accordingly, the Examiner is respectfully requested to withdraw the rejection under 35 U.S.C. § 102.

C. Rejections under 35 U.S.C. § 103(a)

To establish a prima facie case of obviousness, each of the following three criteria must be met. (MPEP 2143). First, the prior art references (or references when combined) must teach or suggest all the claim limitations. *In re Royka and Martin*, 490 F.2d 981, 180 USPQ 580, 583 (CCPA 1974). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one skilled in the art, to modify the reference or to combine reference teachings. Finally, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success, however, must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991)(citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 [Fed. Cir. 1988]). The examiner bears the burden of establishing a prima facie case of obviousness. *Ex parte Obukowicz*, 27 USPQ2d 1063, 1065 (B.P.A.I. 1993).

The Examiner rejected Claims 96, 98-106, 114, 116-125, 137, and 138, under 35 U.S.C. § 103(a) as being unpatentable over Pedersen *et al.* The Examiner stated:

> **. . . it would have been *prima facie* obvious for one of ordinary skill in the art to modify Pedersen's multi-unit controlled release composition with the expectation of at least similar result[s], since Pedersen teaches the advantageous result in the use of hydrophobic material to control the release rate of active substance throughout the GI tract.**

Applicant respectfully submits that the Examiner has not met his burden of establishing a prima facie case of obviousness.

First, Pedersen *et al.* fails to teach or suggest the claim element of an "active lipid", a limitation recited in each of the subject claims, *e.g.*, independent Claims 96 and 114 and the claims depending therefrom. As stated above in connection with Applicant's remarks relating to the Examiner's 35 U.S.C. § 102 rejection, the "active lipid" claimed in the present application is patentably distinct from the wax-like hydrophobic substance disclosed in Pedersen *et al.* Pedersen *et al.*, in fact, teaches away from including such an element in their controlled release coating composition, as the Pedersen *et al.* formulation relies on the fact that the coating, including the waxy hydrophobic substance, remains intact after enteral delivery, rather than be in predigested or "active" form.

Second, without the hindsight provided by the specification as filed, one of ordinary skill would lack the motivation to modify the chemical properties of Pedersen *et al.*'s wax-like controlled release formulation into a carrier-dispersible form of an active lipid as recited in the present claims (*see, e.g.*, independent Claims 96 and 114 and the claims depending therefrom). As the Examiner accurately notes, Pedersen *et al.* teaches a hydrophobic material, in combination with other substances, to control the release rate of active substance *throughout the GI tract*, **not** in order to trigger the jejunal brake to increase absorption of an active ingredient over the proximal portion of the small intestine. In fact, as stated above, the Pedersen *et al.* controlled release composition is formulated to remain intact after enteral delivery, rather than be in predigested or "active" form.

Finally, because -- absent Applicant's disclosure -- Pedersen *et al.* and the knowledge in the art lack any suggestion or motivation to modify the Pedersen *et al.* wax-like composition to comprise an "active lipid," there can be no expectation, let alone reasonable expectation, of success.

For the foregoing reasons, at least, Applicant respectfully submits that the Examiner has not met his burden of establishing a prima facie case of obviousness and respectfully requests the Examiner to withdraw the rejection.

The Examiner also rejected Claims 96, 114, and 118, under 35 U.S.C. § 103(a) as being unpatentable over the combination of Pedersen *et al.* and U.S. Patent No. 5,411,751 granted to Crissinger *et al.* The Examiner stated:

> **Crissinger teaches the use of (C_{16}-C_{22}) fatty acid[s] in food product[s] to reduce GI irritation (abstract). The food product further comprising vitamins and minerals (column 3). Thus, it would have been obvious for one of ordinary skill in the art to prepare Pedersen's composition using the fatty acid in view of the teaching of Crissinger, because the references teach the advantageous result in the use of fatty acid. The expected result would be [a] controlled release dosage form useful in pharmaceutical and/or food products.**

At the outset, Applicant respectfully disagrees with the Examiner's characterization of Crissinger *et al.* as teaching "the advantageous result in the use of fatty acid" "to reduce GI irritation." On the contrary, the cited reference teaches an infant food product where the *ill effects* of fatty acids on infant epithelium are disclosed. (*See* Crissinger *et al.* Abstract). In fact, Crissinger *et al.* teaches an infant food product *free* of both (C_{16}-C_{22}) fatty acids and triglycerides of (C_{16}-C_{22}) fatty acids, or which contains only "subirritant amounts" of these, together with an ester component consisting of "lower alkyl esters" of (C_{16}-C_{22}) fatty acids. Moreover, the fatty acids discussed in Crissinger *et al.* are noted generally for their nutritive value, not for their ability to trigger the jejunal brake and thereby influence the rate and location of absorption of other substances.

In light of the foregoing, one of ordinary skill in the art would lack motivation to combine the controlled release composition of Pedersen *et al.* with the infant formula of Crissinger *et al.* to arrive at the compositions recited in Claims 96, 114, and 188 of the present application.

For the foregoing reasons, the Examiner is respectfully requested to withdraw the rejection under 35 U.S.C. § 103(a).

D. Conclusion

In view of the above remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,

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